# A Strategy for Efficiently Collecting Aerosol Condensate Using Silica Fibers: Application to Carbonyl Emissions from E-Cigarettes

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ABSTRACT: Analyzing harmful constituents in e-cigarette aerosols typically involves adopting a methodology used for analyzing tobacco smoke. Cambridge filter pads (CFP) are the basis of numerous protocols for analyzing the various classes of compounds representing 93 harmful and potentially harmful constituents identified in tobacco smoke by the FDA. This paper describes a simplified method for trapping the low volatility components of e-cigarette aerosols using a single trapping procedure followed by physical extraction. The trap is a plug of amorphous silica fibers (0.75 g of 4 μm diameter) within a 10 mL syringe inserted between the e-cigarette mouthpiece and the pump of the vaping machine. The method is evaluated for emissions from three generations of e-cigarette device (Kanger-tech CE4, EVOD, and Subox Mini-C). On average, the silica wool traps about 94% of the vaporized liquid mass in the three devices and higher levels of condensate is retained before reaching saturation compared with CFP. The condensate is then physically extracted from the silica wool plug using a centrifuge. Condensate is then available for use directly in multiple analytical procedures or toxicological experiments. The method is tested by comparison with published analyses of carbonyls, among the most potent toxicants and carcinogens in e-cigarette emissions. Ranges for HPLC-DAD analyses of carbonyl-DNPH derivatives in a laboratory formulation of e-liquid are formaldehyde (0.182 ± 0.023 to 9.896 ± 0.709 μg puff^{-1}), acetaldehyde (0.059 ± 0.005 to 0.791 ± 0.073 μg puff^{-1}), and propionaldehyde (0.008 ± 0.0001 to 0.033 ± 0.023 μg puff^{-1}); other carbonyls are identified and quantified. Carbonyl concentrations are also consistent with published experiments showing marked increases with variable power settings (10W to 50W). Compared with CFPs, e-cigarette aerosol collection by silica wool requires only one vaping session for multiple analyte groups, traps more condensate per puff, and collects more condensate before saturation.
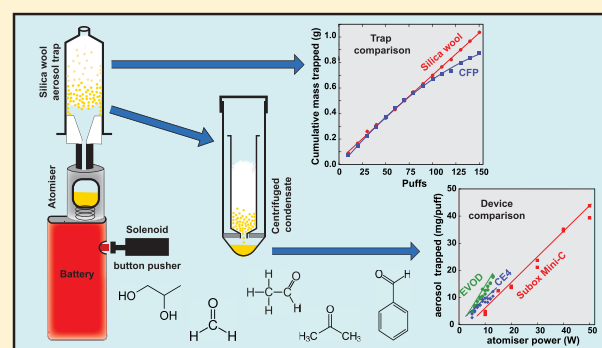
1. INTRODUCTION

The extent that inhaling the aerosol created by vaping e-cigarettes harms the health of users (and bystanders) is widely debated, particularly in comparison with the well-established and substantial health risks of inhaling cigarette smoke.[1,2] The health risks of combustible cigarette smoke and e-cigarette emissions are often compared using the relative differences in toxic emissions and to compare these exposures with published safety limits.[3] The approach most commonly taken to analyzing e-cigarette emissions is to replicate the methods used for analyzing simulated cigarette smoking, yet while some compounds are common to both, the aerosols resulting from tobacco combustion are chemically very different from an aerosolized solution of nicotine as used in e-cigarettes.[4] Conventionally the condensed fraction of the aerosol is collected on a Cambridge filter pad (CFP) and pads are collected separately for each of the various analytical methods. This is an onerous requirement. "Heavy" vaping generates considerably larger quantities of aerosol involving more puffs and/or larger volumes per puff associated with "direct to lung"

inhalation compared with smaller volume "mouth to lung" inhalation typical of smoking combustible cigarettes as well as "light" vaping.[2,5] In this paper the aerosol sampling methodology is addressed for condensates, recognizing the need to sample considerably larger quantities of aerosol and the desirability of simplifying the number of sampling steps for multiple analytical procedures. The condensed fraction of e-cigarette emissions is also important in conducting toxicological exposure experiments, either in diluted or undiluted form.[6]

Most studies of e-cigarette emissions begin with creating the aerosol by simulating human vaping on a device similar to a laboratory smoking machine, followed by trapping the aerosol for chemical analysis.[7] Commonly this involves trapping the condensate, by far the largest fraction of the aerosol by mass, on a filter pad typically followed by extraction using a solvent, sometimes with derivatizing agent. Because the most

appropriate solvent or derivatizing agent tends to be specific to a group of analytes it is usually necessary to use several solvent extraction procedures, requiring the condensate to be trapped repeatedly for each analyte group.[4] Analysis of the full list of the FDA's "Harmful and Potentially Harmful Constituents"[8] and several additional chemical species found within e-cigarette emissions involves numerous discrete methods, usually organized in groups of analytes. One example employs a protocol of 10 separate procedures to extract condensate directly from filter pads and a further 11 to extract from filter pads immersed in impinger solutions, among 27 individual procedures for analyzing e-cigarette emissions.[4] Such meticulous approaches when applied by reputable independent laboratories are essential for setting benchmarks for health protection, but the time and cost of acquiring such comprehensive analyses are beyond the resources of many research laboratories. Simplifying the step that requires multiple batches of condensate for each analyte group could reduce the demand on such resources.

The CFP is a glass fiber or amorphous silica filter pad which is removed from its housing after trapping and the compounds of interest extracted with solvents.[9] The filter sampling method has been criticized within the tobacco industry for lack of accuracy due to inherent losses when the filter pad is removed from its housing.[9] CFPs are also limited in their capacity to retain condensate before becoming saturated, which usually occurs after machine-smoking a few cigarettes.

The possibility that e-cigarette particulates can be collected directly as undiluted condensate without chemical intervention has recently been explored. A single stage method was developed for directly collecting condensed e-cigarette emissions along a pathway of connected modified pipet tips on the principle that a long path length and the funnel effect would combine to condense useful quantities of aerosol.[10] About 40% of vaped liquid has been recovered as undiluted condensate in experiments with this configuration. Another method uses a series of tracheal suction traps in which condensate collects; the efficiency of this method is quoted as 61% by volume.[6] A condensate sample using a high recovery method is likely to be a closer representation of the emission's particulate fraction than a sample obtained using a low recovery method. The most volatile compounds that escape in the gas phase represent a small component of the whole emission in mass terms and comprise dominantly ambient oxygen and nitrogen.[11,12]

The concept developed here aims for greater collection efficiency using a two-stage approach to trap and recover the condensate. In the first stage the liquid phase of the aerosol condensate is trapped in a porous medium and on its container walls (compounds in the gas phase may be trapped downstream in an impinger solution or sorbent cartridge). This is followed by a second stage in which condensate liquid is released and collected from the porous medium under centrifugal force.

The choice of the porous trapping medium is influenced by various factors. The filter must be sufficiently permeable such that resistance to aerosol flow does not adversely impede escape of the gas phases while longer travel paths increase the probability of condensate forming at ambient temperatures and becoming trapped in the porous medium. Extended path lengths are favored by a high degree of tortuosity that provides opportunities for condensation and the collection of liquid droplets, particularly at sites where free flow is impeded.[13]

Such conditions are well satisfied by fine fibrous material in relatively loose and randomly oriented bundles. The second stage requires a relatively open structure so that liquid may be separated efficiently from the porous host medium by centrifuge. Both stages require the host medium to be chemically inert and the viscosity of the liquid condensate must be sufficiently low to facilitate efficient extraction using physical methods.

Here we report the results of using a condensate trap composed of a plug of lightly compressed fine strands (4 μm diameter) of amorphous silica in a form resembling a plug of cotton wool (commercially known as silica wool), along with its recovery from the plug using a centrifuge. As will be shown, this plug and its container typically trap more than 90% of the liquid mass lost to the aerosol during the process of vaping. In this study we used a laboratory prepared e-liquid composed of propylene glycol, glycerol, and water, without any flavorings or nicotine. It is well established that flavorings and nicotine influence e-liquid pH,[14] but the presence of small quantities of these components is not expected to significantly affect the efficiency of condensate trapping. For this reason, a simple formulation of e-liquid (propylene glycol, glycerol, and water) has been chosen to develop the new trapping method; these components are known to degrade at high temperature to low molecular weight compounds including carcinogens, as observed in the emissions of commercial products.[15,16] This trapping method is validated by comparison with the conventional method of trapping particulates as condensate in a CFP. Silica fiber rather than glass fiber CFPs were used for the purpose of comparison with silica wool.

Interlaboratory variability in reported emissions is an issue of some concern, particularly in relation to the highly toxic carbonyls.[17] No reference e-cigarette and e-liquid combination is yet available that provides reproducible emissions under well-defined conditions of puffing and device settings. Research is underway to develop bespoke products that will eventually satisfy the need for reference standards for vaping emissions, but until such time we have resorted to comparing analyses of carbonyls in condensates with the results of broadly similar experiments in the literature. We used three different devices of different e-cigarette generations set to different power settings. Carbonyls were chosen for the comparison exercise, as they are commonly identified among the most potent toxicants and carcinogens in the literature on e-cigarette emissions and their aerosol concentrations can vary considerably depending on factors such as power applied to the atomizer coil.[15,18−24]

2. EXPERIMENTAL PROCEDURES

2.1. Chemicals and Reagents. Glycerol and propylene glycol used for sample preparation, 2,4-dinitrophenylhydrazine phosphoric acid solution, 2,4-dinitrophenylhydrazones of formaldehyde, acetaldehyde, acrolein, acetone, propionaldehyde, crotonaldehyde, methyl ethyl ketone, *n*-butyraldehyde, methacrolein, benzaldehyde, valeraldehyde, *m*-tolualdehyde, and hexanal were obtained from Sigma-Aldrich (Dorset, UK). Pure nicotine was obtained from Acros Organics. Trizma base (tris(hydroxymethyl)aminomethane ACS reagent grade), and elution solvents for HPLC analysis, such as acetonitrile, methanol, and water, all HPLC grade, were purchased from Fisher Scientific (Loughborough, UK). Fibrous 4 μm silica ("silica wool") was obtained from H. Baumbach & Co Ltd. (Suffolk, UK), and Whatman 47 mm QMA silica and glass fiber filters were obtained from Sigma-Aldrich. Both silica wool and QMA filters were checked for surface contamination by treating samples with

Figure 1. Schematic outline of vapor collection and recovery. A: Power to the atomizer is synchronized with the inhalation cycle of a syringe pump (electronics omitted for simplicity). The aerosol is drawn via the mouthpiece into the open end of a 10 mL syringe packed with a plug of silica wool which traps the particulate fraction. B: Silica wool plug contained in syringe after 50 puffs of vaping an e-liquid spiked with green food coloring. Enlargement shows condensed aerosol droplets on the syringe walls and silica strands of the plug. C: Liquid condensate is recovered by centrifuging the syringe containing the silica wool within a 50 mL centrifuge tube centered on a hole in an acrylic disc located above the tapering end of the tube where separated liquid collects.

acetonitrile and Milli-Q water. No evidence of contamination was found in either product.

2.2. Sample Preparation. The same e-liquid formulation was used in all the experiments and was prepared in the laboratory using propylene glycol (PG), glycerol (G), and Milli-Q water. Because of the high viscosity of both PG and G, the e-liquid was gravimetrically prepared by weighing each component in ratio 70:20:10, respectively. For this reason, 16.83 g of PG, 5.85 g of G, and 2.32 g of Milli-Q water were weighed using a high precision analytical balance to a final volume of 25 mL. The solution was then vortexed for 1 min, sonicated for 3 min to remove bubbles of air, and stored at 4 °C until further use.

2.3. Atomizing Devices, Laboratory Vaping, and Aerosol Collection. Three commercial devices were selected to represent the range of noncigalike e-cigarette products popular among UK users.[25] KangerTech CE4 is a clearomizer device with a top coil arrangement for the atomizer, KangerTech EVOD is a bottom coil clearomizer, and KangerTech Subox Mini C is a tank-style device with adjustable power "mod" (often termed and "advanced personal vaporizer"). The Subox Mini C was chosen because the atomizing coil is easily removed for visual inspection without disturbing the tank containing the e-liquid. Coils of 1.8 ohms resistance were used for the CE4 and EVOD devices, and power was supplied from a controllable external supply. The Subox Mini-C included the SSOCC atomizer of 1.5 ohms powered by its own battery in pass-through mode to minimize fluctuations in voltage due to battery depletion. A square wave puff profile was used for all experiments. The wicks supplied with the CE4 and EVOD atomizers were strings of silica while cotton was used for wicking the SSOCC atomizers in the Subox Mini-C. No significant difference was found for trapping efficiency between vertically and horizontally aligned atomizers although alignment can affect the mass of liquid vaped.

Condensate was collected for each run by passing the aerosol through 0.75 g of silica wool into a plug contained in a 10 mL syringe

with a luer tip. Syringes were attached to the mouthpieces of the chosen vaporizers using customized airtight connectors machined from a rod of PTFE. A solenoid valve between the silica wool-containing syringe and the syringe pump directed inflow from the e-cigarette device through the silica plug and the exhalation outflow was directed to exhaust, thus mimicking inhalation−exhalation cycles. An airflow meter placed between the solenoid and the silica wool plugs enables the velocity of aerosol flow emerging from the trap to be monitored. Before and after each run, the atomizer−liquid reservoir and syringe were weighed, and the syringe and its plug were then placed in a freezer at −20 °C for storage until extraction. The condensate collected is dominated by low volatility compounds but may also contain a substantial fraction of volatile components which partition strongly into the aqueous component of the aerosol particulates. Carbonyls would partition in this manner if there is a significant aqueous component to the aerosol. Figure 1A shows the schematic arrangement of components (omitting the electronics controller for simplicity). The pump, solenoids and atomizer power supply, and controller are part of the Gram Universal Vaping Machine package (UVM, Gram Health Inc., USA).

2.4. Recovery of Condensate from Silica Wool. Condensate is trapped in the form of small droplets on the syringe walls and on strands of silica wool as highlighted by green food coloring added to the e-liquid for illustrative purposes (Figure 1B). Recovering this aerosol from the silica plug and its container was achieved by placing the 10 mL syringe within a 50 mL centrifuge tube above an acrylic spacer with a central hole for the syringe tip (the syringe lugs may need to be trimmed to fit into the tube). The spacer holds the syringe several millimeters above the bottom of the centrifuge tube and creates an empty volume in which the extracted liquid collects (Figure 1C). The assembly was spun in a centrifuge for 5 min at 4700 rpm after which the tube was removed and the liquid recovered by inserting a pipet tip through the hole in the disk and transferred to a 2 mL vial. This was immediately sealed and stored at −20 °C until

required. Collecting and storing condensate means that aliquots can be used for different groups of analytes; unstable species such as some carbonyls can be extracted immediately whereas other more stable compounds may remain in the condensate at −20 °C until required. Moreover, the collected samples in undiluted form can be divided in several aliquots and diluted with water or any other solvent suitable for toxicological analysis. To test the efficiency of the condensate recovery, the laboratory e-liquid was spiked with various ketones and aldehydes including acetone, formaldehyde, and acetaldehyde (50 μg mL^{-1} each) to achieve a final concentration within the range of their calibration curves. This spiked e-liquid (1.5 mL) was pipetted into the silica wool plug and vortexed for 20 s. It was then centrifuged under the same conditions as the previous experiments.

2.5. Run Conditions. Fifty puffs of 55 mL were drawn over 4 s and repeated every 30 s. The coil was heated over this interval, but no preheating was applied. This regimen falls within the range of current vaping topography studies.[20] Each atomizer was vaped at a series of voltages that represented incremental increases in power. At the end of each session, the atomizer was removed, and the coil and wick were examined under a microscope (Leitz EZ4HD) to determine the extent of changes to the wick and coil materials (Figure 2). These
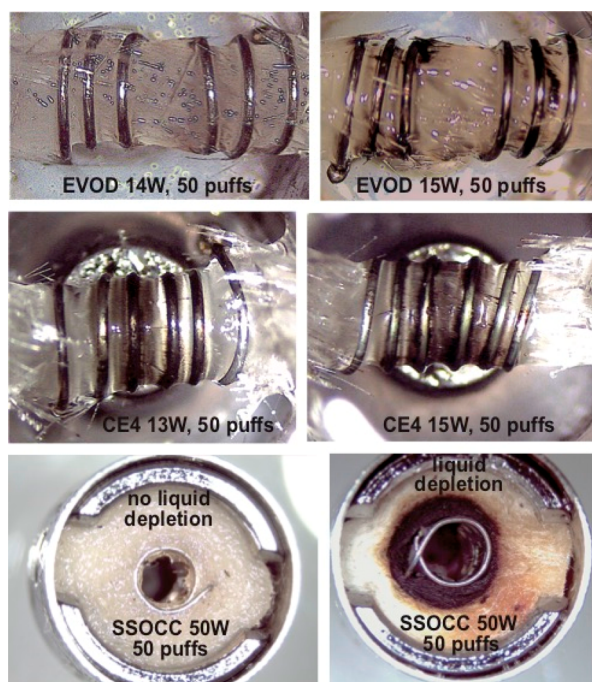
Figure 2. Coil response to power setting and the availability of liquid. The EVOD coil shows little evidence of dark deposits on the silica wick at 14 W but these begin to appear at 15 W. The CE4 coil shows slight darkening of the silica wick at 13 W but there is a marked increase in these deposits at 15 W. The cotton wick of the SSOCC atomizer shows no damage to the cotton wick even at 50 W if the supply of liquid keeps the wick−coil interface wet throughout the run, but when the liquid supply fails during the vaping session, then burning can be extensive.

changes include black/brown solid deposits from overheated e-liquids and the effects of charring cotton wicks. Such deposits could attenuate the supply of liquid to the coil and thus lead to changes in thermal conditions and products of vaporization.[26,27] The choice of maximum power applied to any coil in subsequent experiments was based on the highest voltage that did not give rise to visible deposits on the wicks. This qualitative parameter is not used as a proxy for coil overheating but rather to ensure that coils and wicks are in broadly comparable states for the duration of an experiment. Atomizers were routinely replaced after each vaping session.

2.6. HPLC Analysis. A solution of 13 target compounds was used for identification and quantification of carbonyls in e-liquid and aerosol samples. Calibration curves were prepared in the concentration range 0.06−3.00 μg mL^{-1} in acetonitrile. Both e-liquid and condensed vapor were diluted in acetonitrile (1:10). To allow for detection of carbonyls, analyses were carried out according to CORESTA method 74 with some modifications.[28] Each sample (50 μL) was derivatized using the reaction with 2,4-DNPH (20 μL; 0.02 M) for 25 min. The reaction allows the formation of carbonyl 2,4-dinitrophenylhydrazones which are detectable by high performance liquid chromatography coupled to a diode array detector (HPLC-DAD). Samples were stabilized with Trizma base solution (acetonitrile/aqueous Trizma 80:20) and chromatographically analyzed. The HPLC-DAD system consists of a Thermo Scientific Dionex UltiMate 3000 system (Fisher Scientific, Loughborough, UK), composed of a degassing device, an ASI-100 automated sample injector, and a PDA-100 photodiode array detector set at a wavelength of 365 nm. Chromatographic separation was achieved using a Raptor C18 (150 × 4.6 mm, 2.7 μm) column (Thames Restek, UK Ltd.). The column temperature was set at 40 °C, and the injection volume was 5 μL. Separation was achieved running an elution gradient composed of two solvents: A, ultrahigh purity water; B, acetonitrile and methanol (1:14), in the following order: 0.00 min 30% A; 10.00 min 25.0% A; 16.00 min 10% A; 16.01 min 0% A; 17.00 min 0% A; 17.01 min 30% A; 22.00 min 30% A. Flow rate was set to a constant 0.6 mL/min. The limits of detection (LOD) and the limits of quantitation (LOQ) are given in Table 1 with estimation based upon a signal-to-noise ratio of 3 and 10, respectively. Results were converted to μg puff^{-1} by using the density of the liquid samples.

2.7. LC-MS Identification. The DNPH-derivatized products of carbonyls were further confirmed using liquid chromatography coupled with mass spectrometry according to the method of Lv et al. with some modification.[29] The system was equipped with a LC20ADXR pump, SIL30AC, auto sampler, CTO20A column oven, and a triple quadrupole mass spectrometer (LCMS-8040, all Shimadzu Corporation, Japan). The chromatography conditions were the same as used in the HPLC method described above with injection of 5 μL. The ion source used electrospray ionization (ESI), and parameters were as follows: nebulizer gas flow 3 L min^{-1}, DL temperature 250 °C, heat block temperature 400 °C, drying gas flow 15 L min^{-1}, dwell time 5 ms. The mass spectrometer was operated in negative ion mode using LabSolutions software version 5.93 (Shimadzu Corporation) in multiple reaction monitoring mode. Identification was achieved using the pure standard compound mixture also used for HPLC analysis.

2.8. Statistical Analysis. All samples were analyzed in triplicate, and results are presented as mean values ± standard deviation of detected compounds in both liquid and condensed vapor generated from e-cigarettes. Data were analyzed by ANOVA using XLSTAT (version 2014.5.03, Addinsoft, NY). Significant differences between the samples with a confidence interval of 95% were determined using Duncan's multiple.

3. RESULTS AND DISCUSSION

3.1. Optimizing the Mass for Silica Wool Plugs Used for Condensate Trapping. Using silica fibers to trap e-cigarette aerosol condensate is a novel approach, and there is no guidance on the optimal quantity of silica wool that maximizes trapping without adversely increasing flow resistance. A series of experiments was conducted using different quantities of silica wool loosely packed into a 10 mL syringe, beginning with 0.125 g and increasing to 1.0 g in increments of 0.125 g (approximate weights, accurately measured). Weight lost at the atomizer and weight gained by the trapping syringe were used to calculate the aerosol trapping efficiency, and the experiment was applied to all three atomizer devices operating at 13 W (CE4 and EVOD) and 15 W (Subox Mini-C). These data are used to compare the performance of configurations

Table 1. Analytical Parameters for the Determination of Carbonyls in Condensed E-Cigarette Aerosols (note that compounds are listed as DNPH derivatives)[a]

compound	RT (min)	regression equation[b]	R^2	LOD ($\mu g\ mL^{-1}$)	LOQ ($\mu g\ mL^{-1}$)
formaldehyde	3.86	$y = 1.2713x + 0.0844$	0.991	0.051	0.171
acetaldehyde	4.74	$y = 1.0431x + 0.0482$	0.9928	0.040	0.135
acetone	6.26	$y = 0.8167x + 0.0344$	0.9923	0.051	0.171
propionaldehyde	6.54	$y = 0.7979x + 0.033$	0.9907	0.035	0.115
valeraldehyde	12.42	$y = 0.5466x + 0.0156$	0.9924	0.078	0.258

[a]Limits of detection (LOD) and quantification (LOQ) are given in μg per mL of the certified reference standard. [b]y is the peak area; x is the concentration of carbonyl ($\mu g\ mL^{-1}$).

and devices in capturing the particulate fraction of the aerosol but are not used for mass balance purposes, as the whole aerosol was not analyzed. Mass changes resulting from dehydration or oxidation reactions have not been taken into account but estimates based on extreme values in the literature indicate that this effect would be much less than the error inherent in the measurement.

The results are summarized in Figure 3 which clusters together the various experiments on all three devices for a
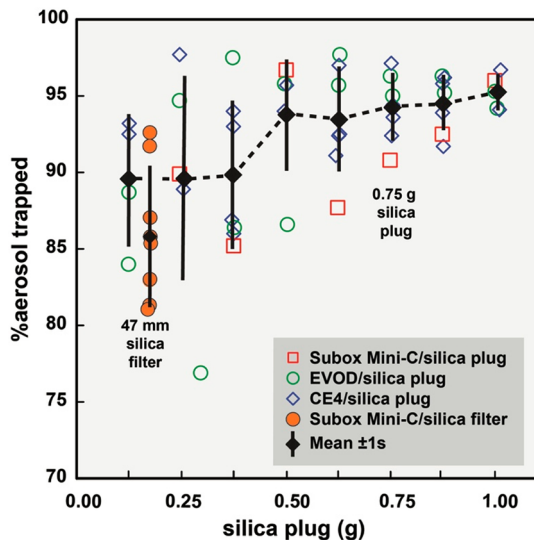
Figure 3. Role of filler mass on the efficiency of aerosol trapping. Colored open symbols represent experiments of 50 puffs using three different vaping devices coupled to a collection syringe packed with plugs of different masses of silica wool. The colored dot represents an analogous experiment using a 47 mm silica filter pad in an air sampling holder. Solid diamond symbols and solid lines represent the mean trapping efficiency (in %) ± 1 s for approximately the same mass of silica with the dashed line connecting the means for the silica plug experiments.

given weight of silica wool plug. Low weights (0.125−0.375 g) trap on average about 90% of the e-liquid mass lost to vaping but with very large variability. Silica masses of 0.5 g and above trap on average approaching 95% of the aerosol with steadily decreasing variance as the mass of silica wool increases. A plug of less than 0.5 g is sufficiently porous to allow the passage of significant amounts particulate-bearing aerosol without trapping. The data indicate that a silica plug of 0.75 g traps at least 90% of vaporized liquid aerosol in 95% of experimental runs. Increasing the mass of silica wool beyond 0.75 g reduces the variance in the mass of liquid trapped but does not significantly increase recovery (Figure 3). The aerosol flow rate declines only slightly with increased plug mass, <3% between 0.15 g

(approximately the mass of a 47 mm CFP) and 0.75 g. For these reasons, 0.75 g plugs were used in all subsequent experiments.

The trapping efficiency of aerosol vaporized from the same e-liquid formulation and collected in 0.75 g silica plugs was essentially identical for the different devices within error. Mean (standard deviation) values over 50 puffs are CE4 94.5% (3.3), $n = 80$; EVOD 94.2% (2.2), $n = 30$; and SuboxMini-C 94.3% (4.3), $n = 18$. The mean for CFPs trapping experiments is 86.9% (3.5).

Silica wool plugs and CFPs (47 mm diameter) were also compared in terms of numbers of puffs in an experiment that vaporized the laboratory e-liquid using the Subox Mini C device and measured the rate of aerosol flow, weight loss of e-liquid, and weight gain of trap with each increment of 10 puffs over 150 puffs. Figure 4A shows the change in flow rate of the aerosol as a percentage of the flow rate measured without a trap. The silica wool plug shows no significant decrease in flow rate as the filter accumulates more condensate over 150 puffs, over which interval 1.1 g of liquid was consumed. In contrast, CFP shows a marked decline to around 60% after 70 puffs (0.54 g of liquid vaped). This decline in flow rate is accompanied by a loss in trapping efficiency, particularly noticeable from about 90 puffs (during which 0.67 g of liquid was consumed (Figure 4B). These data indicate that the trapping performance of silica wool plugs and CFPs is essentially identical until approximately 0.5 g of liquid is consumed, after which the flow rate declines. When 0.7 g of liquid has been vaped, the trapping efficiency of CFP begins to decline significantly whereas the silica wool plug continues to trap condensate linearly up to at least 1 g of liquid consumed. A second CFP housing was placed in series to determine the point of condensate saturation in the filter, as indicated by condensate carryover into the second filter. This occurred at about 1.1 g of liquid consumed. The equivalent experiment with 0.75 g of silica wool in each of two syringes in series found that saturation and carryover was not reached until 6.4 g of e-liquid had been consumed. An experiment to determine whether glass fiber filters have different trapping efficiencies from silica fiber filters showed no significant difference ($p < 0.05$, $n = 14$).

For each of the above experiments using silica wool, the condensate was recovered using a centrifuge as described in section 2.4. Mean recovery of condensate is 81.1% (standard deviation = 10.7) expressed as the fraction of mass extracted by centrifuge from the trap to the mass of aerosol accumulated in the trap; thus, condensate recovered for analysis is typically around 75% of the total aerosol generated by the atomizer. Of the remainder, a fraction is difficult to extract from the silica plug without the use of solvents and a further fraction of volatile degradation products escapes into the gas phase which
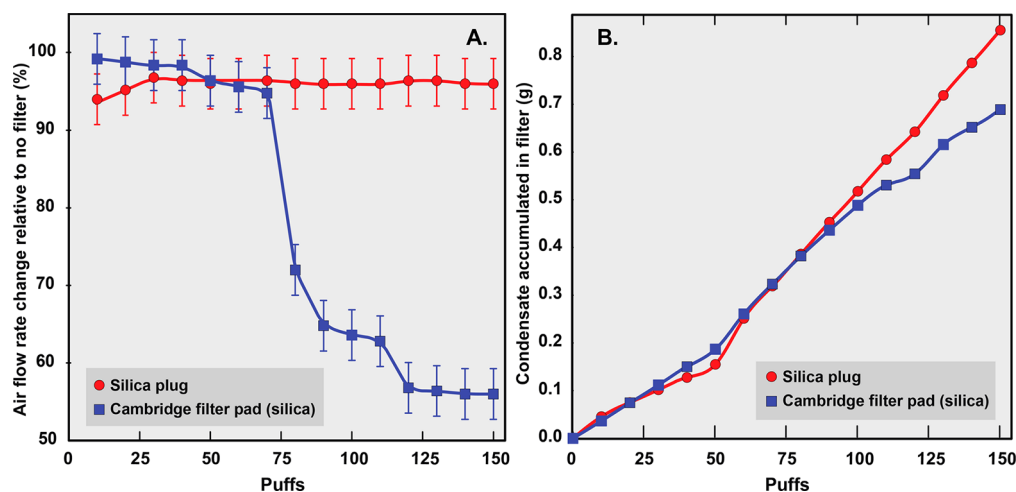
Figure 4. A: Percentage variation in aerosol flow rate with puff number relative to unobstructed airflow (i.e., no filter) for silica plug and Cambridge filter pad (error bars are one standard deviation of triplicate measurements). B: Cumulative mass of condensate trapped with puff number for silica plug and Cambridge filter pad.

also includes ambient nitrogen and oxygen.[11] In conventional analysis of whole tobacco smoke the CFP is often removed after the experiment and immersed in the downstream impinger solution. The same procedure is possible with silica wool plugs with or without the centrifuge stage (centrifuging is preferred as it creates a dry plug that can be removed intact without leaving residual condensate smeared on the syringe walls).

The question arises as to whether the model e-liquid used in these experiments adequately represents factors such as viscosity and surface tension in commercially available e-liquids with nicotine and flavorings that may influence the trapping of condensates. The model e-liquid was replicated with nicotine added to create a liquid with 18 mg mL^{-1} nicotine. The model liquid and the model liquid with nicotine had the same trapping efficiencies ($p = 0.05$, $n = 12$). Six flavored commercial e-liquids were purchased (tobacco, menthol, coffee, apple, lemon, and cream flavors). The trapping efficiencies of all six were found to fall within the range of two standard deviations of the mean for the model e-liquid. We found no statistical evidence that nicotine and flavorant additives substantially change the trapping efficiencies of e-liquids.

3.2. Effect of Variable Power on Vapor Generation. It is well established that greater power supplied to atomizer coils results in greater quantities of e-liquid vaporization.[18,20,26] Figure 5 shows the results of experiments in which the three devices were used at various powers up to, but not beyond, the threshold of significant wick changes as determined by visual inspection (note that these thresholds refer to 4 s duration puffs with no preheating). The CE4 and EVOD atomizers showed no evidence of deposits at 13 W, but both began to show evidence of deposit build-up at 15 W; however, no changes were observed in the Subox Mini-C SSOCC atomizer, even at 50 W, and adequate e-liquid supply appears to have been continuous throughout the session. In early experiments when the liquid was exhausted prior to completing the session, there was considerable charring of the cotton wick (Figure 2). To avoid charring, the SSOCC (cotton) wick was pierced with a needle through the atomizer side-openings where the cotton is in contact with the liquid reservoir, as recommended on the web by numerous users of this atomizer, and under these
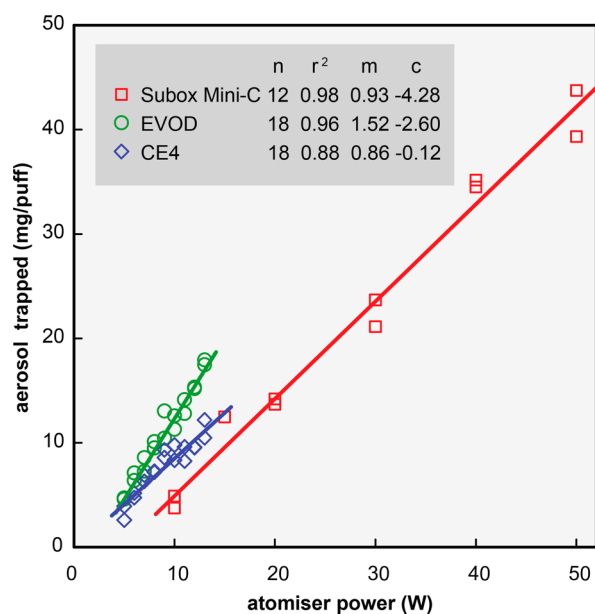

Figure 5. Production of aerosol condensate (mg/puff) as a function of atomizer power (W) for three devices nominally of 1.5 and 1.8 ohms resistance. Puffs are 55 mL. Power increments ceased when an atomizer showed evidence of damage such as burning or charring.

conditions there was no evidence of charring or any coil-related deposits over many sessions.

Each device describes a distinct linear trend of increasing aerosol trapped with power (Figure 5). Gillman et al. found that devices operating between 5 and 25 W yielded up to 28 mg of aerosol per puff at the highest powers.[30] The present work used the same vaping regimen and found similar aerosol yields up to 25 W, extending the range of liquid consumed to 47 mg per puff at 50 W.

It is noteworthy that the mass of aerosol trapped from the Subox Mini-C device is well correlated ($r^2 = 0.98$) with atomizer power (Figure 5). Before the cotton wicks were pierced to improve the flow of liquid to the SSOCC coils, the cotton wrap showed signs of significant charring after two or three 50-puff sessions, even at lower powers. The linear trend was only made possible by intervening to ensure that

Table 2. LC and MS−MS Identification of Different DNPH-Carbonyls with Their Retention Time, Molecular Mass, [M − H]⁻, and Fragment Ions

compounds	retention time (min)	molecular mass (amu)	DNPH derivative [M − H]⁻ (m/z)	fragment ion for qualification (m/z)	collision energy
formaldehyde	3.67	30.0	209.00	163.20; 151.20	9; 9
acetaldehyde	4.67	44.0	223.00	163.20; 151.20	11; 10
acetone	6.02	58.0	237.10	207.30; 151.20	10; 9
propionaldehyde	6.25	58.0	237.05	163.20; 152.20	11; 15
valeraldehyde	9.99	86.1	265.05	152.25; 80.00	17; 54

Table 3. Identified Carbonyls and Their Concentrations (μg puff⁻¹) in the Condensed Samples Vaped at Different Powers Using CE4, EVOD, and Subox Mini-C Devices[a]

	F (μg puff⁻¹)	AA (μg puff⁻¹)	A (μg puff⁻¹)	P (μg puff⁻¹)	V (μg puff⁻¹)	other carbonyls[b] (μg puff⁻¹)	mass vaped (g), [N puffs]
CE4							
15 W	9.649 ± 3.082[a]	0.178 ± 0.0247[c]	0.0363 ± 0.003[cd]	0.018 ± 0.007[ab]	0.562 ± 0.205[b]	12.899 ± 1.775[b]	0.563 ± 0.04, [50]
EVOD							
13 W	2.901 ± 0.471[b]	0.157 ± 0.0006[c]	0.047 ± 0.005[cd]	0.008 ± 0.0001[b]	0.345 ± 0.018[bc]	2.793 ± 0.341[cd]	0.377 ± 0.004, [50]
15 W	4.103 ± 1.236[ab]	0.124 ± 0.0007[ce]	0.025 ± 0.0007[d]	0.008 ± 0.002[b]	0.286 ± 0.0005[bc]	2.942 ± 0.291[cd]	0.283 ± 0.004, [50]
Subox							
10 W	0.182 ± 0.023[b]	0.059 ± 0.005[e]	0.030 ± 0.007[d]	nd	0.005 ± 0.0001[c]	0.606 ± 0.117[d]	0.266 ± 0.04, [50]
15 W	0.433 ± 0.080[b]	0.131 ± 0.022[ce]	0.054 ± 0.007[c]	<LOQ	0.035 ± 0.010[c]	1.110 ± 0.079[d]	0.473 ± 0.23, [50]
30 W	3.375 ± 0.495[ab]	0.298 ± 0.007[b]	0.132 ± 0.009[b]	0.008 ± 0.001[b]	0.257 ± 0.061[bc]	7.114 ± 0.047[c]	1.18 ± 0.004, [50]
50 W	9.896 ± 0.709[a]	0.791 ± 0.073[a]	0.318 ± 0.001[a]	0.033 ± 0.023[a]	1.098 ± 0.216[a]	30.011 ± 3.956[a]	1.40 ± 0.04, [30]

[a]Data for the mass vaped over a given number of puffs is included to facilitate conversion to other units. nd = not detected; <LOQ = below limit of quantification; F, formaldehyde; AA, acetaldehyde; A, acetone; P, propionaldehyde; V, valeraldehyde. Data are reported as average of replicates ± standard deviation. Lower case letter superscripts indicate significant differences ($p < 0.05$) using Duncan's test. [b]Unidentified carbonyl peaks detected in the chromatograms were summed and reported as "other carbonyls".

replenishment of liquid kept pace with the consumption of liquid by piercing the tight cotton wrap. The slope for the EVOD device is steeper up to 13 W, beyond which wick deposits were observed, suggesting that this is a more efficient vaporizing device but with limited fluid replenishment capability.

3.3. Carbonyl Identification and Quantification. Earlier studies involved the chromatographic separation of carbonyl compounds with similar structures and polarity.[19] In this study, several C18 columns of different length and pore size were tested using different gradients and elution solvents to seek improved separation of the standard mixture of 13 carbonyls. Previous trials failed to achieve complete separation; for example, peaks of acrolein and acetone coeluted at the same retention time as peaks of methacrolein, methyl ethyl ketone, and butyraldehyde, giving a broad peak. Under the conditions used in this study, an effective gradient separation was achieved for compounds with very similar chemical properties.

Each carbonyl in the standard mixture was identified based on its retention time, peak shape, and UV-spectra. A confirmation assay was also performed by LC-MS/MS in ESI (−) mode, which showed the molecular ions of each carbonyl-DNPH derivative that have lost one proton giving [M − H]⁻. The fragment ions selected for identification of DNPH derivatives are listed in Table 2. The laboratory e-liquid formulation was analyzed using HPLC, but no peaks were detected except for that of the derivatizing agent (DNPH, RT = 2.82 min). However, in the condensate samples more than 10 peaks were detected, and some of these were identified as specific carbonyls by reference to standard compounds, while some hitherto unknown peaks were summed and reported as other carbonyls. To estimate repeatability and reproducibility, six replicates of two levels of sample were run for intra- and

interday experiments using HPLC. Precision was determined by percent coefficient of variation (CV) calculated as follows: CV (%) = (standard deviation/mean) × 100. Accuracy was calculated as percent bias: Bias (%) = [(calculated concentration − theoretical concentration)/theoretical concentration] × 100. Acceptance criteria for both accuracy and precision are defined by FDA Guidelines for Bioanalytical Method Validation.[31] The calculated values for CV% and the bias% were lower than 15% and ranged between ±15% of nominal concentrations, respectively.

Carbonyls are relatively unstable compounds. We performed HPLC analysis on samples stored at room temperature and also at −20 °C to limit the loss of volatiles. No significant difference was detected between these samples. Repeated HPLC analysis of two vaped samples of different concentration for six consecutive days and storing the samples at −20 °C indicated that they differed by less than ±15% from the nominal concentration. Thus, the compounds of interest appear to be stable for at least for 6 days when stored at −20 °C.

To test the recovery using the physical extraction through centrifugation, the spiked e-liquid was analyzed before and after centrifugation. The results demonstrated good recovery for all carbonyls (96.5% ± 0.03, 89.6% ± 0.14, and 93.2% ± 0.03, for acetone, formaldehyde, and acetaldehyde, respectively). Formaldehyde showed the lowest recovery, most probably because it has the lowest boiling point. Table 3 shows the carbonyls identified with their concentrations in μg puff⁻¹ of the condensed samples after vaporizing at different powers for CE4, EVOD, and Subox Mini-C devices. These results for carbonyls are in agreement with literature data;[21,32] in particular, formaldehyde ranges from 0.182 ± 0.023 to 9.896 ± 0.709 μg puff⁻¹ and acetaldehyde ranges from 0.059 ± 0.005 to 0.791 ± 0.073 μg puff⁻¹. However, care must be taken when

comparing carbonyl concentrations from published data, as the devices and run conditions are often very different; furthermore, the units in which concentrations are expressed also vary (e.g., mass/volume; mass/mass; mass/puff). The data presented in Table 3 should enable conversion to other units.

The results show that among devices, Subox produced lower concentrations of carbonyls at 15 W followed by EVOD and CE4. In particular, CE4 showed a 2-fold increase in total carbonyls. This is to be expected as CE4 was vaporized using 2 s coil preheating prior to puffing whereas the EVOD coil was not preheated. Both atomizers showed some microscopic evidence of coil damage and wick deposits at 15 W suggesting that the carbonyl levels may be enhanced if liquid replenishment had been inadequate.

3.4. Variation in Carbonyl Generation with Device Type and Voltage (power). The phenomenon of "dry puffs" is widely recognized as likely to increase the toxicity of the emitted aerosols mainly due to higher levels of carbonyls, although it is possible that the high formaldehyde concentrations in these emissions is likely to make the emissions unpalatable to vapers.[33,34] The observed changes in wicks subjected to high power vaporizing may derive from charring or even combustion of the wick when it is fabricated with combustible materials (e.g., cotton) or as caramelized and charred degradation products of e-liquids accumulating as deposits on and within the wick surfaces (Figure 2). Silica wicks are essentially inert, and the commonly observed dark deposits on these wicks are most likely the thermal degradation products of e-liquids. By clogging the capillary property of wicks, such deposits will eventually lead to attenuated liquid supply and thus increase the likelihood of dry puffs. The coils may also show evidence of corrosion and buckling. The liquids collected in the experiments of section 2.4 (Figure 2) bracket the advent of deposit formation on wicks in the CE4 and EVOD atomizers at 13 W and 15 W, respectively.

With regard to the carbonyls, Table 3 shows that as the power setting increases from 13 W to 15 W (EVOD) and from 10 W to 50 W (Subox Mini-C) the devices generate higher concentrations of selected carbonyls, as previously observed.[22] As well as power, additional factors appear to be significant in carbonyl generation including coil surface area[27] and metal catalysis.[35] The 2-fold increase in total carbonyls in CE4 may be accounted for, at least in part, by the 2 s preheating of the coil in advance of puffing whereas the EVOD coil was not preheated. Both coils showed microscopic evidence of deposits at 15 W suggesting the involvement of overheating in the enhanced carbonyl levels. Formaldehyde in the Subox aerosol increases from 0.182 ± 0.023 μg puff^{-1} to 9.896 ± 0.709 μg puff^{-1} over the range 10 W to 50 W. Interestingly, the concentration of all carbonyls released from Subox at 30 W is still lower than those reported at 15 W released from the other devices, although the mass of aerosol generated at 30 W is greater (Figure 5). This suggests that if wicking in the Subox Mini-C device operates efficiently, the device can produce relatively high levels of toxic compounds at high power with no evidence of coil changes or wick deposits, whereas high levels in both CE4 and EVOD devices are associated with deposits on the wicks.

3.5. Comments on Carbonyl Partitioning in E-Cigarette Aerosols. Partitioning of a carbonyl between gas and particulate phases in aerosols where the particulate phase is composed entirely of organic compounds is essentially determined by the vapor pressure, and this indicates that the smaller carbonyls are dominantly partitioned into the gas phase.[36] Partitioning in the presence of an aqueous droplet component of the particulate phase in which carbonyls are soluble or miscible may be determined using values from Henry's Law. Values for the smaller carbonyl monomers indicate a strong partitioning into the aqueous particulate phase; however, the situation is more complex because carbonyls readily form hydrates and oligomers which are less volatile than the monomer and have a greater affinity for the aqueous phase. The foregoing indicates that the presence of water in the e-liquid may have a profound effect on how the vaper is exposed to carbonyls in the emitted aerosol; water-deficient aerosols deliver carbonyls primarily in the gas phase, but water-rich aerosols deliver carbonyls (plus their hydrates and/or oligomers) primarily in the aqueous component of the particulate phase. The relevance of this conclusion is that computational models for the deposition and translocation of inhaled e-cigarette emissions in the human body indicates that gas (vapor)-phase compounds are absorbed mainly in the upper airways whereas particulate phase compounds may also penetrate the lower airwa;,[37] thus, the presence/absence of free water in the aerosol may be a key factor in the absorption of carbonyls in the respiratory system and consequently in carbonyl toxicity.

Few studies have measured the quantity of water in both e-liquid and aerosol, but the available evidence suggests that water is transferred quantitatively into the aerosol.[38] Secondary water may also be generated by dehydration reactions.[39] The carbonyls present in the condensates of this study (Table 3) indicate that a substantial fraction is partitioned into the aqueous particulate phase of the aerosol which is consistent with the e-liquid used in these experiments comprising 10% deionized water (by mass) with 67% propylene glycol and 23% glycerol. The water content of the e-liquid thus determines the dominant phase for carbonyl transfer and is relevant to the choice of aerosol trapping method for carbonyls.

3.6. Limitations. This laboratory-based study suffers from the limitation of all such simulations due to the uncertainties of accurately representing human vaping topography.[40] Furthermore, the model e-liquid used in these experiments is based only on PG, VG, and water and contains no nicotine, flavorings, or other additives. Although these additional components appear to have no significant effect on the trapping efficiency, they are likely to affect chemical and perhaps other attributes. Modeling mass balance and apportioning compounds to aerosol components require condensate collection to be supplemented with means of collecting and analyzing the gaseous fraction of the aerosol and measuring the water content of the condensate fraction.

4. CONCLUSIONS

An alternative to the conventional filter pad method for the collection of e-cigarette aerosol condensate is described. The method is based on trapping the condensate within a plug of silica wool and extracting the liquid using a centrifuge.

The optimal mass of silica wool plug contained in a 10 mL syringe was found to be approximately 0.75 g. This mass did not significantly reduce the flow rate of the aerosol compared with the rate without a filter, and the flow rate did not decline over long puffing experiments. A mean trapping efficiency of 94.3% ($s = 3.3$) was obtained over three e-cigarette devices whereas a similar experiment using 47 mm CFPs gave an efficiency of 86.9% ($s = 3.5$).

Saturation of traps is a problem when aerosols transfer large masses of particulates or when a large number of puffs are required. The 47 mm CFP saturated with breakthrough at a load of 1.1 g whereas saturation did not occur until 6.4 g of condensate in the silica wool trap, although using a much larger diameter CFP could overcome this problem.

The efficiency of extracting the condensate from the silica wool plug by centrifuge is 81.1% (10.7). This is representative of the whole condensate as demonstrated by analyzing an e-liquid sample spiked with known concentrations of carbonyls and dispersed within the silica wool plug and then recovered using the same centrifuge method.

The raw condensate extracted from the plug of silica wool without solvent is suitable for use directly in multiple analytical procedures, whereas conventional methods require multiple filters to be collected to accommodate the wide range of extraction procedures tailored for particular groups of analytes. The condensate may also be stored for use in toxicology exposure experiments.

Silica wool-based and CFP-based methods may be hybridized. Thus, silica wool may be removed from the syringe and placed in impinger solution, as is common in many procedures using CFPs. This imparts to conventional procedures the trapping advantages of silica wool in comparison with CPFs, as identified above.

The variable power aspect of this study supports the view that the substantial cancer risks attributable to formaldehyde and acetaldehyde in the e-cigarette emissions are largely a function of high-power settings. Finding that accumulation of wick deposits coincides with increased carbonyl emission offers the possibility that experiments that have generated results with clogged wicks can be identified post hoc and their results interpreted accordingly. This awaits further research. It has been suggested that "dry puffs" associated with exceptionally high carbonyl concentrations can be identified by vapers, although this remains controversial,[22,34,41] and a simple visual test of wicking inefficiency may provide useful complementary information during laboratory testing of e-cigarettes. The absence of wick deposits or burning in cotton wicks at very high-power settings indicates that carbonyl emissions can increase to high levels even when wicks appear to be well supplied with e-liquid.

Analysis of carbonyls in the vaporized aerosol of e-cigarettes is important for assessing the potential risks of cancer and other diseases from vaping compared with smoking,[3] and this study links a published analytical protocol with a novel and improved sampling methodology that does not require expensive laboratory infrastructure.

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